

RESTRICTED

CIRCULAR LETTER NUMBER 4

MANAGEMENT OF THE VENEREAL DISEASES

HEADQUARTERS
MEITERRANEAN THEATER OF OPERATIONS
UNITED STATES ARMY
OFFICE OF THE SURGEON
APO 512

25 JANUARY 1945

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I - INTRODUCTION

1. The following outline on the diagnosis, treatment, management and follow up of the venereal diseases is published as a guide to be followed by all medical officers in this theater who are called upon to treat venereal diseases. Since substantial changes from previous methods are here recommended, it should be carefully studied.

2. All previous Circular Letters dealing with the diagnosis and treatment of venereal diseases, Office of the Surgeon, MTOUSA and NATOUSA, *are rescinded*:

Circular Letter Number 10, dated 10 April 1943

Circular Letter Number 14, dated 18 May 1943

Section I Circular Letter Number 28, dated 20 August 1943

Section III Circular Letter Number 6, dated 21 January 1944

Circular Letter Number 20, dated 29 March 1944

Circular Letter Number 38, dated 8 July 1944

Section VI Circular letter Number 44, dated 22 August 1944

Section III Circular Letter Number 53, dated 8 November 1944

3. All previous Circular Letters dealing with the diagnosis and treatment of venereal diseases, Office of the Surgeon, SOS NATOUSA and COMZONE, MTOUSA *are rescinded*:

Technical Medical Bulletin No. 7, Sec. IV dated 24 April 1944

Technical Medical Bulletin No. 16, Sec. I and IV, dated 15 June 1944

II - GENERAL POLICIES

A - Hospitalization policies.

1. All military personnel requiring diagnosis and treatment for venereal disease will, when indicated, be promptly hospitalized in the venereal disease treatment centers operated for that purpose. In areas where such facilities do not exist, they will be hospitalized in station or general hospitals. Penicillin therapy for syphilis will be administered only in venereal disease treatment centers or hospitals. Base Sections, Armies, or Air Force Surgeons should designate certain facilities as venereal disease treatment centers. Penile ulcers may be treated

on a duty status provided the diagnosis of syphilis has been excluded. The unit medical officer will continue the treatment of syphilis in those cases in which the Mapharsen-Bismuth routine is used.

B - Hospital organization (venereal disease section).

1. The hospital management of patients with venereal disease ordinarily entails the use of diagnostic, epidemiologic and administrative procedures which are similar regardless of the specific type of venereal disease.

2. In hospitals in which a venereal diseases section is indicated, it will be organized as a unit of the Medical rather than of the Surgical service.

C - Flying personnel.

1. Because of the possibility of altered physiological reactions as the result of sulfonamide treatment, flight surgeons will give special attention to such cases and will base their decisions regarding these cases on a consideration of the following:

- a) Previous history of sulfonamide reactions,
- b) Nature of individuals flight duties,
- c) Nature of flight contemplated,
- d) Dosage being administered, and
- e) Any other pertinent considerations.

D - Line of duty.

Reference is made to War Department Circular Number 458, dated 2 December 1944 for determination of line of duty status. Patients hospitalized for spinal puncture following treatment for syphilis or for diagnostic purposes will be recorded as « yes » on all medical reports.

E - Toilets.

Since venereal diseases are seldom if ever, transmitted from one individual to another through the medium of toilets, there is no rationale for employing separate toilets for venereal diseases cases. The adoption of such a policy is generally to be discouraged.

F - Serology.

It cannot be emphasized too much that serologic tests are *only an aid* in the diagnosis of syphilis. Great care must be exercised in making a diagnosis of syphilis based solely on positive serology. Decisions regarding diagnosis and treatment must be made on the basis of all available evidence, history, physical examination previous therapy and laboratory tests. Consultation will be utilized when considered necessary.

G - Follow up of venereal cases.

1. FOLLOW UP.

All individuals who have developed venereal disease will be followed to determine cure, or the development of other of the venereal diseases, as outlined under each of the diseases of this directive.

2. ROSTERS.

In accordance with AR 40-210, dated 15 September 1942, as revised by Section I, War Department Circular Number 410, dated 19 October 1944, a list or roster, of all venereal patients who are undergoing treatment or follow up but who are not excused from duty, will be maintained both by the organization commander and by the surgeon.

3. ENTRIES ON THE INDIVIDUAL'S SERVICE RECORD.

a) In accordance with Change 7, dated 24 November 1943, of AR 40-210, dated 15 September 1942, as amended by Section III, War Department Circular Number 397, dated 9 October 1944, the surgeon will notify the custodian of the individual's Service Record that a syphilis register on the individual exists at the hospital or dispensary, *who upon receipt of such information from the Surgeon will cause to be entered under administrative remarks of the service record the following notation: « W.D., MD Form No. 78 or W.D., AGO Form No. 8-114 (formerly Form No. 78) (Syphilis Register) is a part of this person's records ».*

b) *The following notation will be entered in the service record of individuals who are being followed up for gonorrhea, syphilis, chancroid, lymphogranuloma venereum and granuloma inguinale, in accordance with Section . . . , paragraph . . . (enter name of the venereal disease and date).*

4. TRANSFER.

a) In the event of transfer of the individual, the syphilis register will be obtained from the Surgeon and forwarded with the service record and allied papers direct to his new station or command.

b) The unit surgeon will check the service record of each new arrival in his unit and the individuals to be followed up will be added both to the Surgeon's and the organization commander's venereal disease roster.

H - Unit notification of venereal disease case.

Upon discharge of a venereal patient from a medical installation, notification of such fact in writing will be furnished the unit surgeon, through the unit commanding officer, in accordance with paragraph . . . Section . . . Circular Letter No. . . . Headquarters,

MTOUSA, dated . . . Information will be furnished on a form which will include name of patient; army serial number; laboratory tests performed with the results, such as serology, darkfields, smears, etc.; final diagnosis; total number of days hospitalized (lost from

duty) as a result of observation and treatment of this venereal disease; treatment given as penicillin (units), sulfonamides or other and a statement indicating that the case has been reported on this organization's W.D. 86ab report as new, old or formal transfer.

III - DIAGNOSIS, TREATMENT AND FOLLOW UP OF SYPHILIS

A - Diagnosis.

1. It is of the utmost importance that the diagnosis in primary and secondary syphilis be established at the earliest practicable moment and that treatment be instituted as soon as the diagnosis is made. Approved definitions and standard nomenclature are listed in Section IX of this directive.

2. A DIAGNOSIS OF SYPHILIS WILL BE MADE:

a) Upon demonstration of motile *Treponema pallidum* by darkfield examination certified by a medical officer. The presence of spirochaetes other than *Treponema pallidum* in oral and anal lesions renders material from these sources *unreliable* in the diagnosis of syphilis.

b) In the presence of typical clinical manifestations, a diagnosis of syphilis will be made on the basis of two positive reactions to the standard Kahn test.

3. FALSE POSITIVE SEROLOGY AND APPRAISAL IN QUESTIONABLE CASES.

a) Many individuals in the Armed Forces have been treated for syphilis solely on the basis of positive reactions disclosed by routine serologic examinations in the course of, or immediately following, a non-syphilitic disease.

b) Serodiagnostic tests are not truly specific for syphilis. Many non-syphilitic conditions produce frequent or occasional false positive serologic reactions; 30 or more conditions have been enumerated. Some of the conditions that produce transient false positive reactions are:

(1) Technical false positive reactions. Not usually confirmed when rechecked with a different test or when a second specimen is retested with the same procedure.

(2) Vaccinia and vaccinoid reactions. Positive serology usually disappears in 3 months. Other immunizations may perhaps give false positive reactions.

(3) Upper respiratory infections, atypical pneumonia, influenza, bronchitis, lobar pneumonia, etc. Majority usually become seronegative within 3 months after the onset of the disease.

(4) Leprosy.

(5) Malaria. There is some evidence to indicate that all patients with malaria may develop a false positive serologic reaction sometime during the course of the disease.

(6) Typhus (epidemic and murine).

(7) Weil's disease and infectious hepatitis.

(8) Infectious mononucleosis.

(9) Lymphogranuloma Venereum.

(10) Fever and other diseases.

c) Verification Tests.

No present verification test meets all requirements necessary to differentiate the biologic false positive from the true syphilitic serologic reactions. Verification tests will not be used as a serodiagnostic procedure.

d) In the absence of typical clinical manifestations a diagnosis of syphilis should not be made on the basis of positive serologic tests until the individual has been thoroughly studied. Treatment for syphilis should be withheld until certain conditions other than syphilis are ruled out.

e) *Duration of False Positive Reactions.* Some individuals may continue to give false positive serologic reactions for several years for no apparent reason. The majority of serums become negative within 3 to 4 months.

f) Suggestions for appraisal.

(1) Detailed history.

(2) Complete physical examination. Radiologic studies of the heart and aorta are desirable.

(3) Spinal fluid examination.

(4) Repeat serologic examinations. Every 2 to 4 weeks for a minimum period of 3 months. At the end of this time a complete re-appraisal to determine wheth-

er or not syphilis may be present. Quantitative serology is helpful.

(5) Additional laboratory examinations should include blood counts, blood smears, tests for infectious mononucleosis, etc.

g) At the end of the 3 or 4 month observation period, the patient should be completely re-appraised to determine whether or not syphilis may be present. In this re-appraisal, the following considerations will apply:

(1) Those in whom the serology has reversed to and remained negative will be discharged as non-syphilitic.

(2) Those individuals having a persistently positive reaction to tests on successive specimens will be diagnosed as syphilis and treated.

(3) Those still having conflicting serology with no clinical evidence of syphilis may be subjected to further serologic and clinical follow-up. This group represents one of the most difficult problems in syphilology, and wherever possible, consultation should be obtained prior to final disposition.

h) It must be remembered that false positive serologic reactions may occur during the post treatment follow up period in individuals that have been treated for syphilis. A reversal of the serology from negative to positive should be investigated carefully before labelling this condition as serologic relapse.

4. YAWS, PINTA and BEJEL.

It should be borne in mind that positive serologic tests occur in certain other treponemal diseases such as yaws, pinta, and bejel.

5. « PRESUMPTIVE » OR « EXCLUSION » TESTS will not be used in the diagnosis of syphilis.

6. LUMBAR SPINAL PUNCTURE will be routinely employed for withdrawal of spinal fluid as a diagnostic or therapeutic procedure. Cisternal puncture will be used *only* in those cases where lumbar puncture has proved unsuccessful because of spinal block or other pathologic condition and will never be employed for the withdrawal of spinal fluid in syphilis cases for routine analysis. Spinal punctures will be performed only in hospitals or venereal disease treatment centers.

B - Treatment of syphilis.

I. GENERAL PRINCIPLES OF TREATMENT.

a) Penicillin will be the drug of choice in the treat-

ment of certain types of syphilis as outlined in the succeeding paragraphs.

b) Arsenoxide (mapharsen) will be used as the standard arsenical when penicillin is not obtainable or its use inadvisable. No other arsenical will be used in these cases.

c) Each treatment is to be recorded on the Syphilis Register of the patient, or if for any reason a Syphilis Register is not available, a written record is to be kept and transferred to the standard form as soon as possible. Each entry will include date, drug, dose, and reaction.

d) Patients that have been started on mapharsen-bismuth therapy will not be changed to penicillin therapy except as enumerated in B 2 (4) (5) below.

2. PENICILLIN TREATMENT OF SYPHILIS.

a) *Indications for Penicillin Treatment of Syphilis.* Penicillin will be used in the treatment of the following types of syphilis:

(1) *Untreated primary and secondary syphilis.* (Mapharsen-bismuth treatment has not been initiated.)

(2) *Untreated latent syphilis.* (Mapharsen-bismuth treatment has not been initiated.) It is essential that a preliminary spinal fluid examination be made in all cases of presumed latent syphilis. If the spinal fluid is abnormal the case must be classified as asymptomatic neurosyphilis and be managed according to Section IV, this directive.

(3) *Acute Syphilitic Meningitis.*

(4) *Treated primary and secondary syphilis which has failed to respond to mapharsen-bismuth therapy.* This includes:

(a) Clinical relapse, such as mucocutaneous, ocular, osseous, or visceral.

(b) Treatment-resistance, a rare condition manifested by failure of the primary and secondary lesions to respond to adequate mapharsen-bismuth therapy, usually accompanied by the presence of living treponemes in the lesions.

(c) Serologic relapse as evidenced by reversal of a negative STS (serologic test for syphilis) at the conclusion of mapharsen-bismuth therapy to positive during the 6 months post-treatment observation period. Criteria of serologic relapse are discussed later.

(d) Serum-fastness as evidenced by a persistent positive STS at the end of mapharsen-bismuth therapy.

(5) *Treated primary, secondary, and latent syphilis intolerant or sensitive to mapharsen-bismuth therapy.*

This group includes individuals who have had a serious reaction to arsenic that contraindicates its further use. Arsenical jaundice, exfoliative dermatitis, a blood dyscrasia (thrombocytopenic purpura, agranulocytosis, aplastic anemia) and encephalopathy are examples of such reactions. Patients who manifest persistent intolerance of less serious character, such as severe headaches, nausea, vomiting and diarrhea, even with reduced doses of mapharsen, may also be included.

b) Technique of Penicillin Treatment of Syphilis.

(1) *Facilities and personnel.* Penicillin therapy requires hospitalization of approximately 10 days, including 7½ days of therapy, and time consumed for pre-therapeutic diagnostic procedures and administrative details. It is the responsibility of the medical officer in charge to see that adequate supplies of the drug are on hand before actual treatment of the patient is started.

(2) *Dosage and technic of administration of penicillin.* Uniform dosage and technic will be used in all cases. The total dosage will be 2,400,000 units of penicillin, given in 60 consecutive *intramuscular* injections of 40,000 units (2 cubic centimeters of penicillin solution) at 3-hour intervals day and night for 7½ days. Any convenient time schedule may be adopted, but in most army hospitals the most suitable schedule is 0200, 0500, 0800, 1100, 1400, 1700, 2000 and 2300. The solution should be injected intra-muscularly. Good sites are the upper outer quadrant of the buttocks or the deltoids. The needle for injections in the buttocks should be 2 inches to 2½ inches in length, preferably 20-gauge, in order to insure intra-muscular injection rather than injection into fat. *No additional antisyphilitic therapy is to be given during or after the completion of the course of penicillin except in the case of penicillin treatment failures discussed in succeeding paragraphs.*

(3) *Non-interruption of penicillin treatment.* Treatment should continue without interruption after its initiation. On the first day of treatment, commonly, and during the course of treatment less frequently, minor reactions may be encountered. None of these is indication for the discontinuance or interruption of therapy. There have been no instances so far in which it has been necessary to discontinue or interrupt the treatment schedule.

c) Reactions Observed in Penicillin Treatment of Syphilis.

(1) Herxheimer reactions. These occur frequently in cases of primary and secondary syphilis, less commonly in cases of latent syphilis, and rarely in cases that have already received some antisyphilitic therapy. The manifestations may be focal or systemic and are ascribed to the massive destruction of treponemes in the syphilitic lesions and in the blood stream. These reactions may therefore be considered of favorable significance. Both the focal and systemic Herxheimer reactions are encountered on the first day of treatment only. They begin usually some 3 to 6 hours after the first penicillin injection, gradually become worse and reach a peak, after which they slowly and progressively subside, disappearing within an average of 24 hours. No specific therapy is required although such drugs as aspirin and codeine may be given for relief of symptoms. It must be emphasized that these symptoms disappear spontaneously in spite of the continued regular administration of penicillin, and are not justification for discontinuance of therapy.

(a) The focal Herxheimer reaction consists of an aggravation of the existing syphilitic lesions. There may be increased swelling of the chancre, further enlargement of already enlarged regional lymph nodes accompanied by pain, and exaggeration of the secondary eruption. A pallid, sparse, macular eruption often becomes extremely profuse and vividly red, and may resemble measles or scarlet fever.

(b) The systemic Herxheimer reaction may be manifested by a variety of symptoms, such as headache, malaise, nausea, occasionally vomiting, abdominal cramps, and weakness, but its most characteristic features are chilly sensations and fever. Peak temperatures of 105.4 F. have been recorded, although generally lower grades of fever prevail.

(2) *Other Reactions caused by Penicillin.* Other reactions caused by penicillin have been extremely rare and trivial in the dosages recommended herein. Most patients will complain of more or less local muscle soreness at the site of the injections, but usually this has not been objectionable. The most common late systemic reactions have been secondary fever occurring toward the end of treatment and terminating immediately on its cessation; urticaria or other minor skin eruptions; generalized pruritus; herpes labialis and

progenitalis; and mild gastro-intestinal symptoms such as abdominal cramps, nausea, and occasionally vomiting.

d) Post Treatment Observation of Patients Treated for Syphilis with Penicillin.

(1) *Serologic and clinical follow-up.* All syphilis cases treated with Penicillin will have a monthly inspection and STS for a period of 12 months. This will be done by the unit medical officer and the blood sample sent to the nearest medical laboratory, station, or general hospital. Appropriate entries will be recorded in the Syphilis Register and Venereal Disease Follow-Up Files of the unit medical officer.

(a) *Quantitative serologic tests for syphilis.* A quantitative Kahn test will be done on all specimens of blood in which a report *other* than negative is obtained, but quantitative Kahns need not be done during the first 4 months of the follow-up period. The result will be reported in Kahn units.

(2) *Spinal fluid.*

(a) In primary and secondary syphilis the spinal fluid will be examined as soon after the completion of 6 months of observation as feasible. In no case will the syphilis register be closed until this examination has been accomplished.

(b) Spinal fluid tests to be performed. Cell count; Pandy or Nonne-Apelt qualitative tests for protein; quantitative estimation of total protein; complement fixation (Wassermann) test; or, if this is not feasible, a flocculation test; and colloidal gold test. The cell count and Pandy or Nonne-Apelt test should be performed at the local laboratory within 30 minutes after the spinal fluid is withdrawn.

(3) *Special administrative features of penicillin treatment.*

(a) Preparation of the Syphilis Register (W.D., AGO Form No. 8-114) (formerly W.D., MD Form No. 78). Form No. 78 will be used until Form 8-114 is received. This will be filled in completely in the usual manner and a brief note describing the treatment procedure will be made in the register. A sample note reads as follows:

«Soldier received intensive penicillin therapy from 20 June 1944 to 27 June 1944 consisting of 60 consecutive intramuscular injections of 40,000 units at 3-hour intervals for a total dose of 2,400,000 units. There was a febrile Herxheimer reaction the first day with peak

fever of 102.4 F. Lesions were healed when therapy was completed.»

Notation will also be made in the register that the patient is to be managed in accordance with provisions of this Circular Letter.

(b) *Preparation of W.D., MD Form No. 78a (Patient's Record of Syphilis Treatment).* - This will be prepared as a personal record for the soldier. A brief account of the treatment status of the patient will be entered. This can be done simply by repeating the note made in the Syphilis Register, described in (a) above. An additional statement will be made to the effect that no further treatment is required, except in the event of clinical or serologic relapse, but that the patient will have a regular monthly physical examination and blood test. This form can be used as a record of follow-up and a reminder for the soldier by inscribing at each visit the date set for the next examination.

(c) *Closure of the Syphilis Register.*

1 *Primary and secondary syphilis.* The Syphilis Register will be closed in primary and secondary syphilis and transmitted to the Surgeon General after 12 months of observation in all patients who have become and remained serologically negative; who have had no evidence of clinical relapse; and who have had a negative spinal fluid between the completion of 6 months of observation and the time of closing of the register.

2 *Latent syphilis.* The Syphilis Register will be closed in latent syphilis and transmitted to the Surgeon General after 12 months of observation if there has been no clinical or serologic relapse even though the serologic tests have remained persistently positive. It is anticipated that serum-fastness will not be uncommon in cases that receive penicillin therapy in the latent stage of syphilis.

e) Clinical and Serologic Post Treatment Course of Favorably Responding Penicillin Treated Syphilis.

(1) *Primary and secondary syphilis.*

(a) *Clinical course.* - The rate of healing of primary and secondary syphilitic lesions varies, depending principally upon the type of lesion. Ordinarily, simple nonulcerated chancres of small size, mucous patches, and macular eruptions are healed by the time the treatment course is completed. Large ulcerated chancres, deeply infiltrated papular eruptions, and large condylomata lata may not heal completely for 1 to 3 weeks after treatment is concluded. The presence of such

lesions, unless physically incapacitating, or requiring extensive local treatment, will not be cause for prolonged hospitalization.

(b) *Serologic course.* - The titre of the STS declines gradually from positive to negative in the post-treatment period, the negative phase being achieved in a variable time. The majority of cases become negative between the second and fourth post-treatment months, although earlier and later reversals occur. In general, the higher the initial titre of the quantitative STS the longer the test will take to become negative, and the lower the initial titre the sooner the test will become negative.

(c) *Critical relapse period.* - The critical period for relapse, both clinical and serologic, appears on the basis of present information to lie between the third and sixth post-treatment months, although relapses have occasionally been observed at earlier and later periods.

(2) *Latent Syphilis.*

(a) *Clinical course.* Since these patients have no visible syphilitic lesions, no observations as to healing can be made.

(b) *Serologic course.* The serologic curve may take the same course as that observed in primary and secondary syphilis. This is especially true of cases of very early latent syphilis, notably those which have only recently passed from the secondary phase into the phase of latency. On the other hand, individuals with older latent syphilis are likely to exhibit serologic refractoriness, the STS showing either no tendency or little tendency to lose strength. This results in the case having to be classified eventually as serum-fast.

f) *Definition of Penicillin Failure.* - Care should be exercised in the determination of failure since patients may develop intercurrent skin eruptions of non-syphilitic character. Intercurrent infections and small-pox vaccination may produce a temporary elevation of the titre of the quantitative STS. All forms of clinical relapse are generally accompanied by serologic relapse, or by persistently high serologic titres. Treatment failures may be divided into nine categories.

(1) *Mucous and or cutaneous relapse* is manifested by the appearance of syphilitic lesions of the mouth, genitals, and skin, the latter especially in the anogenital region. There may be lesions of both skin and mucous membranes (mucocutaneous relapse), or of either surface alone. Darkfield examinations should be performed

to corroborate the diagnosis. If the darkfield examination is negative, repeated quantitative STS should be performed which will reveal a progressively rising titre. In doubtful cases consultation is desirable.

(2) *Serologic relapse* is manifested by a rising titre of the quantitative STS after the test has become negative or has manifested a previously falling trend. When a serologic relapse is suspected, the patient should be thoroughly and frequently examined, since serologic relapse is usually accompanied or shortly followed by mucocutaneous or some other clinical relapse. Since the titre of the quantitative STS may vary from time to time, as a result of laboratory technic, and in different laboratories, it is not sufficient to accept minor fluctuations in the titre as evidence of serologic relapse. Serologic relapse should be diagnosed only when a series of consecutive tests, performed preferably in the same laboratory, show persistently increasing titres over a period of 3 to 4 weeks. In the event that a titred test is not available a change from a doubtful or negative reaction to a persistently positive reaction will be accepted as adequate evidence of serologic relapse. It should be noted that the titre characteristically rises during, and for a brief period after, penicillin therapy. This elevation is temporary and is not to be considered evidence of serologic relapse.

(3) *Serum fastness* in primary and secondary syphilis is manifested by a failure of the quantitative STS to show a marked decline within an arbitrary period of 6 months after completion of therapy. Minor fluctuations in the titre may be observed, and also a drop to a lower sustained level, but there is no consistent, gradual, and maintained fall to negative. This condition will be uncommon in primary and secondary syphilis, where it will be considered a treatment failure when present 6 months after completion of therapy. *It will not be uncommon in latent syphilis, in which it will not be considered a treatment failure.*

(4) *Neurologic relapse* (neurorecurrence) may occur as acute syphilitic meningitis, with headache, dizzy spells, fever, and rigidity of the neck. In fulminant cases, coma may supervene rather rapidly. Less commonly, relapse in the nervous system may appear as an isolated cranial nerve palsy or paralysis of one or more extremities. Diagnosis should be confirmed by spinal fluid examination. In these cases the neurologist should be consulted for diagnostic assistance.

(5) *Asymptomatic neurosyphilis* is manifested only by an abnormal spinal fluid.

(6) *Ocular relapse* may be manifested by iritis, usually unilateral, or optic neuritis, or neuroretinitis, which may be unilateral or bilateral. The latter conditions may be accompanied by headache, and blurring and progressive failure of vision. In these cases the ophthalmologist should be consulted for diagnostic assistance.

(7) *Osseous relapse* is manifested by severe pain, often nocturnal, in the long bones, most often the tibias, or severe headache when cranial bones are affected. Local tenderness over the affected bone is often very acute. Roentgenograms may assist in the diagnosis.

(8) An extremely rare case may occur which fails to respond immediately to penicillin, where lesions fail to heal and living treponemes are present after completion of the treatment course.

(9) *Other forms* of visceral relapse such as hepatitis have so far not been observed but should be watched for.

g) Management of Penicillin Failures.

(1) Cases of neurologic relapse and asymptomatic neurosyphilis will be managed in accordance with Section IV, this directive.

(2) All forms other than (1) above of treatment failure after the 2,400,000 unit course of penicillin will receive a second course of the drug. This will consist of 4,000,000 units of penicillin, given in 80 consecutive intramuscular injections of 50,000 units at 3 hour intervals day and night for 10 days. These patients will be followed during the post treatment period as described in paragraph B 2 d above. Treatment failures after the second course of penicillin will be transferred to a general hospital in which expert consultation can be obtained for further evaluation and treatment.

3. MAPHARSEN-BISMUTH TREATMENT OF SYPHILIS.

a) *General.* This type of treatment will be administered to those individuals:

(1) That have been started on this schedule.

(2) When penicillin is not available.

(3) To all cases except as listed under paragraph B 2 a, Section III, « Indications for Penicillin Treatment of Syphilis ».

(4) Certain types of neurosyphilis (Section IV).

b) Treatment of Early and Latent Syphilis.

(1) Primary and secondary syphilis and latent syphilis of any duration should be treated by an identical treatment system. This treatment may be completed

within 26 weeks (See Treatment Schedule - Table I).

(2) Patients with syphilis, early or latent, should as a rule, be hospitalized initially to the end that a careful examination may be made and antisyphilitic treatment started. The period of hospitalization need not be prolonged more than 5—7 days. Thereafter treatment should be continued by unit medical officers.

(3) Table I - Treatment Schedule, Primary, Secondary and Latent Syphilis.

Week		
1	Arsenoxide (mapharsen) intravenously twice weekly, total 20 injections.	Bismuth subsalicylate intramuscularly once weekly, 5 doses.
2		
3		
4		
5		
6		
7		
8		
9		
10		
11	Omit arsenoxide (mapharsen) - 6 weeks.	Bismuth subsalicylate intramuscularly once weekly - 6 doses.
12		
13		
14		
15		
16		
17	Arsenoxide (mapharsen) as in first course, twice weekly total 20 injections.	Bismuth subsalicylate intramuscularly once weekly, 5 doses.
18		
19		
20		
21		
22		
23		
24		
25		
26		

Arsenoxide (mapharsen) dosage: the dosages adjusted approximately to the body weight: average dose 60 milligrams, minimum dose 50 milligrams, maximum 70 milligrams.

Bismuth subsalicylate in oil dosage: The standard dose is 0.2 grams of bismuth subsalicylate intramuscularly (not 0.2 grams of elemental bismuth metal).

Technical Suggestions.

(1) Discard discolored drugs and solutions and damaged ampules.

(2) Dissolve arsenoxide in sterile distilled water in the proportion of 10 milligrams of drug per 2 cubic centimeters of water; a dose of 60 milligrams will then be contained in 12 cubic centimeters of solution, 50 milligrams in 10 cubic centimeters, and 70 milligrams in 14 cubic centimeters.

(3) Shake and aerate arsenoxide; do not shake or aerate the other arsenicals.

(4) Inject arsenoxide rapidly to avoid thrombosis; there is little danger of speed shock or nitritoid crisis. Other arsenicals should be injected *slowly* to avoid speed shock or nitritoid crisis.

(5) Thoroughly shake oily suspensions.

(6) Attempt aspiration after insertion of needle before making any injection, especially intramuscularly.

(7) Inject bismuth intramuscularly into upper outer quadrant of buttock. Alternate sides.

(8) Massage firmly after withdrawing needle from buttock and have patient prolong massage to three minutes.

(9) Advise rest if practicable after arsenicals.

(10) Warn patient to report his reactions.

(11) Watch mouth and gums for bismuth stomatitis.

c) *Treatment is to be stopped and the patient hospitalized* if the following appear:

(1) An itchy dermatitis of the face or flexures.

(2) Jaundice.

(3) Petechial or other hemorrhagic lesions.

(4) Evidence of cerebral injury, even though slight.

d) *General Anti-Reaction Therapy.*

(1) Epinephrin solution 1:1000, $\frac{1}{2}$ — 1 cubic centimeter subcutaneously for speed shock or nitritoid crisis.

(2) In cerebral vascular accidents measures to be considered are venesection and hypertonic saline solution intravenously (500 cubic centimeters of a 1.5 percent solution).

(3) In blood dyscrasias, transfusions.

(4) Sodium thiosulphate for any type of treatment reaction is considered valueless.

e) *Follow - Up of Mapharsen-Bismuth Treated Cases.*

(1) *Serologic control of treatment.* In patients with primary and secondary syphilis a serologic test will be done at the beginning and end of the schedule of treatment outlined in table I; but treatment may be stopped whether the serologic test for syphilis (STS) is positive or negative. After the completion of treatment, STS should be repeated three and six months later. If the test is negative after six months and the physical examination is negative the case may be classified as «Result Satisfactory and the *Syphilis Register* may be closed. If the test is positive after six

months, the patient should be referred to a general hospital.

(2) In patients with latent syphilis the STS should be repeated at the completion of treatment outlined in Table I, but the *Syphilis Register* may be closed when this treatment is completed, regardless of the result of serologic test, provided the physical examination is negative.

(3) *Spinal fluid examination* should be performed in a hospital in patients with primary and secondary syphilis at the end of the course of treatment outlined in table I, or as soon as possible thereafter, but in any event before the *Syphilis Register* is closed. In apparent latent syphilis, spinal puncture should be performed in a hospital before treatment is initiated.

f) *Control of Relapse and Infectiousness.*

(1) Early syphilis is to be regarded as infectious until the second injection of arsenoxide has been given. Cases should be returned to duty immediately following the second injection.

(2) Physical inspection of skin (including palms and soles) mucosa, anus, and genitalia should be performed as often as circumstances permit during treatment and at each probationary inspection.

(3) The involution of the chancre or secondaries should be watched to detect treatment-resistant cases.

(4) Patients should be warned to look for and report mouth, skin, and genital lesions. Darkfield examination is of great help in recognizing relapsing lesions of the skin, mucosa, and genitalia.

g) *Complications of Relapse.* In the event of any complication of treatment (serious treatment reactions) or any evidence of relapse, clinical or serologic, the patient should be at once transferred to a general hospital.

h) *Cardiovascular, Visceral, and Neurosyphilis* require special treatment in hospitals.

i) *Treatment of Precocious Late Syphilis* (Tertiary). As soon as possible precocious late syphilis (early gummatous and rupial lesions and bone lesions) should be hospitalized for indicated therapy.

j) *Treatment of Congenital Syphilis.* On recognition or on appearance of active lesions, congenital syphilis should be treated on the schedule for early and latent syphilis. (Mapharsen-bismuth routine).

IV - MANAGEMENT OF NEUROSYPHILIS

A - General.

1. Despite adequate and continuous antisyphilitic treatment, an appreciable number of individuals with syphilis will develop some degree of central nervous system involvement. The management of these patients presents a problem requiring expert diagnosis and treatment. The principles governing the treatment and disposition of individuals with neurosyphilis are summarized herewith.

2. All patients with evidence of asymptomatic or symptomatic neurosyphilis will be transferred to a general hospital for treatment or disposition. The syphilologist in such hospitals will utilize freely consultative advice and assistance available from other sections or services. In patients presenting special problems in diagnosis or treatment, consultation should be obtained.

B - Diagnosis of neurosyphilis.

The following considerations will be taken into account:

1. ASYMPTOMATIC NEUROSYPHILIS. This is neurosyphilis without symptoms or physical (neurologic or psychiatric) signs of the disease; the diagnosis is based

unsupported by other spinal fluid abnormalities, requires repetition before acceptance as evidence for the diagnosis of asymptomatic neurosyphilis. If the Wassermann test is not definitely positive, other tests on the borderline of normality should be repeated after an interval of not less than 2 weeks in order to exclude technical error. In general, the diagnosis of asymptomatic neurosyphilis depends on the interpretation of the pattern of these five tests, rather than on normality or abnormality of any one of them.

b) Asymptomatic neurosyphilis, early or late, may be conveniently divided into three groups, depending on the degree of the spinal fluid changes. Sample patterns of the spinal fluid in these three groups are as follows (These findings apply only to non-bloody spinal fluid):

2. SYMPTOMATIC NEUROSYPHILIS. This diagnosis presumes that the patient has symptoms and or neuropsychiatric signs of disease. In each instance, where symptoms or physical signs suggest such a diagnosis, appropriate serologic examination of blood and cerebro-spinal fluid aid in the clinical classification of the case. From the clinical standpoint, symptomatic neurosyphilis may be divided into five broad categories.

Group	Pattern of Change	WBC per cu/mm	Pandy or Nonne-Apelt	Total Protein	Complement Fixation	Colloidal Gold
I	Minimal	8 or More	Negative or doubtful	5-50 mg per 100 cc	Negative or doubtful	0000000000 to 2221060000
II	Intermediate	8-200 or more	Doubtful to positive	40-100 mg per 100 cc	Doubtful to positive (with 1 cc of fluid)	Any type eg, 2211100000 0012210000 1123100000 3332100000
III	Maximal	8-200 or more	Doubtful to positive	40-200 mg per 100 cc	Positive (with .1 to .5 cc of fluid)	5554321000

on routine examination of the spinal fluid. The tests on which such a diagnosis depends are cell count; Pandy or Nonne-Apelt qualitative tests for protein; quantitative estimation of total protein content; complement fixation (Wassermann) test; and colloidal gold test.

a) *The Wassermann test is the only one of these which is specific for syphilis, and even this test, when*

a) Acute syphilitic meningitis.

b) Diffuse meningovascular neurosyphilis (including such entities as « cerebrospinal syphilis », gumma of the brain or spinal cord, etc.).

c) More or less purely vascular neurosyphilis hemiplegias, hemipareses, etc.).

d) Tabes dorsalis.

e) General paresis.

C - Professional management.

1. GENERAL. Patients in the groups listed in *a*, *b*, and *c*, below should be returned to duty with a recommendation of a trial period of standard chemotherapy for 6 months as recommended in Table I - Mapharsen-Bismuth Treatment Schedule, this directive. If improvement of the spinal fluid is not evident by this time, or if progression has occurred, the patient should be transferred to a general hospital for further study.

a) Early (less than two years' duration of infection) asymptomatic neurosyphilis with Group I and Group II spinal fluid changes.

b) Late (more than 2 years' duration of infection) asymptomatic neurosyphilis with Group I spinal fluid changes.

c) Duration of infection unknown, Groups I and II.

2. ACUTE SYPHILITIC MENINGITIS should be treated with penicillin using the same schedule as recommended for primary and secondary syphilis. Other

types of symptomatic neurosyphilis as meningovascular and vascular should be started on the indicated therapy while waiting to be returned to the Zone of the Interior.

3. FEVER THERAPY. The administration of fever therapy is not applicable to patients in this Theater. Patients requiring fever therapy will be returned to the Zone of the Interior.

D - Disposition.

Individuals with symptomatic neurosyphilis or asymptomatic neurosyphilis, early or late, with Group III spinal fluid abnormalities will be returned immediately to the Zone of the Interior. In addition, individuals with Group I and II asymptomatic neurosyphilis who have not responded to six months of standard chemotherapy following discovery of the positive spinal fluid will also be returned to the Zone of the Interior.

V - DIAGNOSIS, TREATMENT AND FOLLOW UP OF GONORRHEA**A - Diagnosis.****1. DIAGNOSIS IN THE MALE.**

a) *Acute Gonorrhea*. In general, a diagnosis of gonorrhea will be made only when gram negative intracellular diplococci have been demonstrated in smears or cultures of urethral or prostatic secretions. Every reasonable effort will be made by the clinician to demonstrate the gonococcus in smears of urethral discharges. However, treatment should not be withheld too long on account of being unable to do so. The detection of gram negative intracellular diplococci in the urethral exudate, or smears of the centrifuged sediment of the first glass of urine establishes the diagnosis of gonococcal infection.

b) *Chronic Gonorrhea*. (Posterior urethritis, prostatitis, seminal vesiculitis, epididymitis, and arthritis). The detection of gram-negative intra-cellular diplococci in smears of the exudate obtained by digital stripping of the prostate, Cowper's glands, and the urethra, or in smears of the centrifuged sediment of urine passed after stripping the prostate, Cowper's glands, and the urethra, or the demonstration of gonococci in cultures of material so obtained, establishes the diagnosis of gonococcal infection.

2. DIAGNOSIS IN THE FEMALE.

a) The same diagnostic principles as described for the male will be used. Treatment for gonorrhea should be started at once in women who have evidence of this disease, even though laboratory studies are not available. If laboratory facilities are not available, material for subsequent laboratory studies should be obtained before treatment is begun.

b) The detection of gram-negative intracellular diplococci in smears of material obtained from any of the following: the urethra, Skene's glands, or the cervix (or from Bartholin's glands or the rectum, when clinical symptoms exist); or positive cultures of such material establishes the diagnosis of gonococcal infection. (Caution: The normal genital bacterial flora and the flora of non-specific infections may contain organisms that in smear closely resemble gonococci. Therefore, cultural methods should be utilized when possible).

3. GONORRHEAL OPHTHALMIA. The diagnosis is made on the basis of an acute purulent conjunctivitis, pus containing gonococci, and rapid involvement of the external coats of the eye. (Penicillin or sulfonamide therapy should be instituted immediately. Prompt ophthalmologic consultation is imperative).

B - Treatment of gonorrhea.**1. PENICILLIN TREATMENT.**

a) *General.* Penicillin will be the drug of choice in the initial treatment of gonorrhea in both males and females. The use of the sulfonamides will be limited to those cases not responding to adequate penicillin therapy and to those instances in which penicillin is not available through normal supply channels. Penicillin will be administered as promptly as possible after the diagnosis is made. Penicillin therapy may be administered to the patient on a «carded for record only» status (CRO).

b) *Technique.* A satisfactory cure is usually obtained by the administration intra-muscularly of a total of 100,000 units of penicillin divided into 4 or 5 doses given at intervals of three hours. This treatment may be compressed to be given in not less than an 8-hour period.

c) *Failure of Cure from Initial Course of Penicillin Therapy.* In the event of relapse or therapeutic failure, it is advisable that the patient be re-treated with penicillin using the same schedule as above.

d) *Subsequent failures.*

(1) Those patients not responding to a second course of penicillin should be admitted to a venereal disease treatment center or hospital. A prolonged and intensive third course of penicillin totalling not less than 300,000 units and divided into 12-15 doses given at 3-hour intervals should be administered.

(2) Individuals who fail to respond to the third course of penicillin should be treated with one course of sulfadiazine or sulfathiazole, in a dosage of 6 grams initially followed by 1 gram every 4 hours night and day for 5 days.

(3) Individuals who fail to respond to the schedules of treatment mentioned above should be hospitalized for evaluation and further study.

e) *Complications.* Individuals with complications of gonorrhea, such as epididymitis, prostatic abscess, salpingitis, arthritis, ophthalmia, or septicemia, should be hospitalized immediately and treated in consultation with appropriate specialists; larger and prolonged dosage of penicillin such as that recommended in paragraph B 1 d (1), above is necessary.

f) *Non-Specific urethritis.* Patients with urethral discharges in which gram negative intra cellular diplo-

cocci cannot be demonstrated by smears should be treated with penicillin. Many of these cases are gonorrhea in origin but because of the taking of sulfa drugs previously, organisms cannot be demonstrated in smears.

2. **SULFONAMIDE TREATMENT.** In certain instances, it may be impossible or undesirable to treat gonorrhea with penicillin. In these cases, one course of sulfathiazole or sulfadiazine may be administered as follows:

a) *Duty status.* Four (4) grams (60 grains) initially and 1 gram (15 grains) four times a day for 5 days WITH COPIOUS QUANTITIES OF WATER.

b) *Hospital status.* Six (6) grams (90 grains) initially and 1 gram (15 grains) every four hours for 5 days.

3. **LOCAL TREATMENT** of any kind (injections, irrigations, massages, instrumentations) is contraindicated in *uncomplicated acute gonorrhea*.

4. **TREATMENT OF PENICILLIN-SULFONAMIDE RESISTANT GONORRHEA IN MALES AND FEMALES.**

a) *Local Treatment in the Male* (resistant cases only).

(1) When the infection is confined to the anterior urethra, an anterior urethral injection, once daily, of not more than 6 cubic centimeters of a 5 per cent solution of mild protein silver or 0.5 per cent of strong protein silver is advised. (Retain for 5 minute). It should be kept in mind that prolonged use of chemicals tends to perpetuate urethral discharges. Discharges caused by over-treatment of this type may be recognized by the presence of many epithelial cells.

(2) All urethral injections are to be administered by a medical officer or a trained attendant, not by the patient.

(3) Stop all local treatment if the patient develops acute symptoms of posterior urethral infection, such as urgency, painful or marked frequency of urination, or perineal or rectal pain; and confine treatment to hot Sitz baths. When acute symptoms have subsided, resume anterior urethral injections and continue them until prostatic stroking is begun.

(4) Extremely gentle prostatic stroking should be tried when the second glass of urine has been clear, and the first glass nearly so, for two weeks. If gentle massage is painful or causes a recrudescence of other

symptoms, it should not be repeated for one week, or until the symptoms have subsided. If it is not painful and if no recrudescence of symptoms occur, the gland should be gently stripped at three or four day intervals, and smears of the prostatic secretion examined every two weeks. (*When prostatic massage is instituted too soon or applied too vigorously it often induces complications and retards cure.*)

(5) Infections of Cowper's glands should be searched for in resistant cases. If these glands are palpable, they should be gently kneaded. This can be accomplished at the time prostatic massage is practiced, by placing the thumb against the perineum and gently massaging first one and then the other gland with the index finger.

b) Local Treatment in the Female.

(1) In the female, hot vaginal douches (under no more than 2 feet of water pressure) afford comfort and promote cleanliness. Acute pelvic inflammatory disease is an indication for bed rest, ice bags to the abdomen, and analgesics. If enemas are necessary, preliminary bathing of the perineum is indicated before inserting the rectal tube in order to avoid inducing gonococcal proctitis.

(2) The persistence of infection in Skene's glands, Bartholin's glands or the endocervical glands in spite of the use of measures recommended above constitutes a special problem beyond the province of this directive. Such patients require skilled gynecologic treatment.

c) Fever Therapy. In carefully selected cases which persistently fail to respond to other forms of treatment, fever therapy may be instituted. The following methods are recommended for inducing fever:

Interrupted dose, intravenous typhoid.

The intravenous typhoid saline drip.

Hydrotherapy.

C - Determination of cure.

1. IN THE MALE. The number of patients who are not cured with penicillin will be small. Patient treated on a « carded for record only » status should be returned to duty as soon as they are asymptomatic. The presence of an urethral mucoid discharge is not considered of sufficient import to prolong hospitalization,

provided the gonococcus cannot be demonstrated by smear. In every case of gonorrhea, follow up studies should include frequent physical inspections by unit medical officers for 3 weeks after completion of penicillin therapy. Microscopic examinations of urethral discharges, if present, may be made, when indicated. Prostatic massage or urethral instrumentation will ordinarily not be done to obtain material for bacteriologic studies.

2. IN THE FEMALE. Cure will be determined by:

a) Absence of tender masses or points of tenderness.

b) Inability to demonstrate the gonococcus by smears and cultures (when available) in material obtained from the urethra, Skene's glands, Bartholin's glands, or the cervix. Such tests will be repeated on an ambulatory basis at weekly intervals for 3 weeks after disappearance of symptoms and signs. It is recommended that the follow up examination include smears and cultures taken during or immediately following the next menstrual period.

c) To obtain material for smears and cultures, massage the urethra, Bartholin's glands, and Skene's glands, obtaining secretion with small cotton-wrapped applicator or a platinum loop. Pass bivalve vaginal speculum without lubricant, expose cervix, clean vagina, and cervical canal, squeeze cervix between ends of speculum blades, and obtain expressed fluid on cotton applicators or platinum loops for smears and cultures.

D - Follow up.

1. SEROLOGIC TESTS FOR SYPHILIS.

a) It is particularly important that patients with gonorrhea and urethritis, cause undetermined, treated by penicillin be carefully followed with respect to the possible development of primary and secondary syphilis. Since penicillin in adequate dosage is therapeutically effective in early syphilis as well as in gonorrhea, it is possible that the development of primary syphilis may be retarded or masked by penicillin therapy of gonorrhea or urethritis, cause undetermined.

b) It will be the responsibility of the unit medical officer to have blood tests for syphilis performed at the end of the follow up period, and careful clinical and serologic study repeated at the end of 3 months.

VI - DIAGNOSIS, TREATMENT AND FOLLOW UP OF CHANCROID

A - Definition.

« Chancroid is an acute localized autoinoculable, genito-infectious disease acquired usually through sexual intercourse with an infected partner and characterized clinically by necrotizing ulcerations at the site of inoculation. The genital lesions are frequently accompanied by an inflammatory swelling and suppuration of the regional lymph nodes. » - GREENBLATT. The incubation period is a very short one and generally is accepted as 3 to 5 days.

B - Clinical varieties.

1. « The typical single ulceration may be crateriform or have characteristic undermined ragged edges.

2. Multiple ulcerations may result from auto inoculation.

3. Transient chancroid (chancr mou volant) consists of a small superficial ulceration which undergoes spontaneous involution without scar formation in 4 to 6 days. Often, 10 or 20 days after the disappearance of the primary lesion, there may be an acute regional lymphadenopathy followed by suppuration. This transient or evanescent chancroid is rare and may be confused with lymphogranuloma venereum.

4. The phagedenic type (ulcus molle gangrenosum) is a rapidly destructive form of chancroid disease.

5. The giant chancroid has its origin in a simple chancroid lesion which extends peripherally and is featured by extensive ulceration.

6. « The serpiginous type (ulcus molle serpiginosum) spreads by extension and autoinoculation from the original lesions to the groin and thigh. The lesions may spread rapidly. The ulcerations are usually shallow but show no tendency to heal. This form of chancroid may persist for months or years, » - GREENBLATT.

C - Diagnosis.

1. A diagnosis of chancroid may be entertained if the signs and symptoms are typical and if repeated search (a minimum of three negatives on successive days) for treponema pallidum and if frequent blood serologic tests for syphilis yield negative results. Laboratory tests for the diagnosis of chancroid (ITO « Chancroid » skin test or the staining or cultural isolation of the Ducrey bacillus) are not recommended for use in this Theater.

D - Hospitalization.

1. All complicated and or extensive non-syphilitic penile ulcers should be hospitalized until healing processes are well established.

2. UNCOMPLICATED PENILE ULCERS.

a) All penile ulcers will receive 3 darkfield examinations on successive days. In units where these examinations may be secured without excessive use of transportation facilities or interference with duty, they may be carried out on a duty status. In all other instances, penile ulcers will be hospitalized for the necessary period.

b) Patients' status (duty or hospital), following the third negative darkfield will be determined by clinical response, but patients should not be hospitalized until ulcers are completely healed unless definite indication for such procedure exists in the individual case.

E - Treatment.

1. GENERAL. Whether darkfield examinations are carried out on a duty status or in a hospital, oral sulfonamide therapy should be initiated immediately following the first negative darkfield and local therapy should be initiated immediately following the third negative darkfield.

2. ORAL CHEMOTHERAPY.

The sulfonamides (sulfonilamide, sulfathiazole, or sulfadiazine) are specific in the therapy of chancroid. Sulfathiazole is the drug of choice. Two to four grams in divided doses for 7 days is curative in 7 to 12 days in most cases. Occasionally a second course is required. Sulfonilamide seems to be less well tolerated than the others.

3. LOCAL THERAPY.

Sulfonilamide or sulfathiazole powder or 5 per cent sulfathiazole cream should be applied locally.

4. SURGICAL THERAPY.

a) The bubo should never be incised. If fluctuation is present, the bubo should be aspirated and the aspiration point dusted with sulfa powder or 5 per cent sulfathiazole cream applied.

b) Surgical procedure (circumcision or dorsal slit) to relieve phimosis or paraphimosis should be resorted to only on the basis of sound clinical judgment.

F - Follow up.

It will be the responsibility of the unit medical officer to make frequent inspections and blood serologic tests for syphilis for a minimum period of 3 months to make certain that syphilis was not acquired at the same time

as the chancroidal infection. The following schedule is recommended for STS:

1. On admission to sick report.
2. End of first month.
3. End of second month.
4. End of third month.

VII - DIAGNOSIS, TREATMENT, AND FOLLOW UP OF LYMPHOGRANULOMA VENEREUM

A - Definition.

«Lymphogranuloma venereum is a virus disease acquired usually through sexual intercourse with an infected partner and is characterized by a small evanescent initial lesion somewhere on the genitalia which is frequently followed by a subacute regional lymphadenitis.» - GREENBLATT. The usual incubation period is 7-12 days.

B - Diagnosis.

1. The diagnosis should be made on the basis of history and typical clinical manifestations and should be suspected in the presence of acute inflammatory inguinal adenopathy with or without genital ulcers. The FREI test can be considered only an *aid* to diagnosis and the diagnosis of lymphogranuloma venereum will not be made *solely* on the basis of a positive test. The FREI test is of the most value when it is negative, since under these circumstances lymphogranuloma venereum, past or present, may be excluded with reasonable certainty. A diagnosis of lymphogranuloma venereum should not be made on the basis of a positive FREI test in the absence of clinical signs.

2. Darkfield examinations for treponema pallidum will be done on penile ulcers, if present, until a minimum of three negatives on successive days is obtained. Blood serologic tests for syphilis should be repeated at frequent intervals.

C - Treatment.

1. ORAL CHEMOTHERAPY.

The sulfonamides are of some value in the treatment of lymphogranuloma venereum. Sulfathiazole and sulfadiazine are probably the drugs of choice. They may

be administered in doses of 1 gram (15 grains) four times daily for 5 days. It may be necessary to prolong this medication 10 to 14 days, in which case the dose should be reduced to 0.5 grams (7½ grains) four times a day.

2. LOCAL AND SURGICAL THERAPY.

a) Patients with acute inguinal adenitis should be hospitalized whenever possible. The fluctuant buboes should be aspirated, repeatedly, if necessary, but never incised.

b) Excision of the matted gland is permissible and is indicated when the inguinal mass remains chronically indurated for months without signs of suppuration or regression. However, as a general practice, excision is to be avoided because it may be followed by severe elephantiasis of the genitals.

3. THE ACUTE ANORECTAL SYNDROME should be treated in the same manner as the inguinal manifestations. Stricture or other late complications should receive special consideration.

D - Follow up.

It will be the responsibility of the unit medical officer to make frequent physical inspections and blood serologic tests for syphilis for a minimum period of 3 months to make certain that syphilis was not acquired at the same time as the lymphogranuloma venereum infection. The following schedule is recommended for STS:

1. On admission to sick report.
2. End of first month.
3. End of second month.
4. End of third month.

VIII - DIAGNOSIS, TREATMENT AND FOLLOW UP OF GRANULOMA INGUINALE

A - Definition.

Granuloma Inguinale is a chronic granulomatous process which usually occupies the inguinal region and

is caused by infection with a leishmania-like organism. It involves skin and mucous membranes, rarely with coincident adenopathy; it is characterized by vivid-hued,

shining verrucous, vegetating nodules of granulating tissue with a hemorrhagic surface surrounded by a thin, easily excoriated epidermis. The condition spreads by peripheral extension and auto-infection, often involving the entire genital area. It may involve large adjacent areas of the lower abdomen and thighs. The lesions show little or no tendency to spontaneous healing and may persist for months or years.

B - Diagnosis.

1. The clinical appearance of an exuberant, beefy red, velvety tufts of granulation tissue with little or no involvement of the regional lymph nodes is suspicious of granuloma inguinale. The finding of Donovan bodies in deep tissue scrapings stained with Wrights or Giemsa stain or in biopsy material, confirms the diagnosis.

2. Darkfield examinations for treponema pallidum will be done on all lesions of granuloma inguinale until a minimum of 3 negatives on successive days is obtained. Blood serologic tests for syphilis should be repeated at frequent intervals.

C - Treatment.

1. CHEMOTHERAPY. Early granuloma inguinale responds rapidly to therapy with various antimony preparations. The effectiveness decreases in direct proportion to the chronicity of the lesions.

a) *Tartar Emetic*. A freshly prepared 1 per cent solution is more effective. It may be given intravenously in ascending doses with 1 cubic centimeter and increasing the dose by 1 cubic centimeter until a dose of 10 cubic centimeters is reached. It is administered every 2 to 3 days. When the maximum is reached, the dosage

is decreased by 1 cubic centimeter in descending strength until it is reduced to the initial dosage. After a 2 week rest period medication is again started. Toxic manifestations such as joint pains, sore gums, anorexia, nausea and vomiting are often encountered with tartar emetic.

b) *Fuadin* has proved to be superior to tartar emetic. It is more convenient to administer, more stable and toxic reactions are seldom encountered. The initial dose of Fuadin is 1.5 or 3 cubic centimeters intramuscularly. The dosage is then raised to 5 cubic centimeters and given three times per week.

c) *Anthiomaline* is another stable and useful preparation that yields good results in a high percentage of cases. It is administered intramuscularly three times per week.

2. LOCAL TREATMENT of the lesions may be limited to daily dressings.

3. SURGICAL EXCISION of the lesion may be done if the lesions are localized. Large areas may be treated with solid carbon dioxide pencils or radiation therapy.

D - Follow up.

It will be the responsibility of the unit medical officer to make frequent physical inspections and blood serologic tests for syphilis for a minimum of 3 months to make certain that syphilis was not acquired at the same time as the granuloma inguinale infection.

The following schedule for STS is recommended:

1. On admission to sick report.
2. End of first month.
3. End of second month.
4. End of third month.

IX - DIAGNOSTIC NOMENCLATURE FOR SYPHILIS AND DEFINITION OF TERMS

A - Diagnostic nomenclature for syphilis in the army.

Syphilis, primary.

Syphilis, secondary.

Syphilis, early latent (less than four years since infection)

Spinal fluid negative.

Spinal fluid not performed (diagnosis tentative).

Syphilis, late latent (four or more years since infection).

Spinal fluid negative.

Spinal fluid not performed (diagnosis tentative).

Syphilis, tertiary — otherwise unclassified.

Mucocutaneous.

Osseous.

Ocular (except optic atrophy).

Visceral (except cardiovascular).

Cardiovascular-other.

Aneurysm (saccular).

Aortic regurgitation (insufficiency).

- Aortitis (uncomplicated).
- Neurosyphilis - otherwise unclassified.
 - Asymptomatic.
 - Acute syphilitic meningitis.
 - Diffuse meningovascular.
 - Optic atrophy.
 - Tabes dorsalis.
 - Taboparesis.
 - Psychosis with syphilitic meningoencephalitis (general paresis).
 - Psychosis with neurosyphilis other than paresis or taboparesis.
- Syphilis, type undetermined - to include cases in which accurate diagnosis has not been made.
- Syphilis, congenital - include all manifestations.
- Arsenical poisoning.
- Bismuth poisoning.
- Iodine poisoning.
- Mercury poisoning.
- Spinal puncture for diagnosis or progress.
- Special therapeutic practices -
 - Fever therapy - malaria, artificial.

B - Definition of terms and explanations of their use.

1. PRIMARY.

To include those cases presenting the primary lesion of syphilis (the chancre), which have not yet developed secondary manifestation. This diagnosis must be confirmed by darkfield examination, serologic test of the blood, or both. If blood serologic test is negative, the diagnosis of primary syphilis is not permissible without the demonstration of *T. pallidum* by darkfield.

2. SECONDARY.

To include only those cases of early syphilis which show one or more of the manifestations of systemic dissemination of the spirochete; for example, generalized enlargement of lymph glands, cutaneous eruption, mucous patches, condylomata lata, patchy alopecia, laryngitis, bone pains, febrile reaction, and so forth. The chancre may or may not be present and if present may be in any stage of evolution. In early secondary cases, the manifestations of systemic spirochetal dissemination are increasing, have attained their maximum, or are waning. This diagnosis must be confirmed by darkfield examination, serologic test, or both.

In early secondary syphilis and in addition to the

manifestations listed above, ocular or neurologic complications (iritis, neuroretinitis, acute syphilitic meningitis) should be specially recorded as: « Syphilis, secondary, manifested by..... ».

3. LATENT.

Secondary symptoms have subsided and the active manifestations of late syphilis have not yet supervened. There are no evidences of syphilis other than a positive serologic test of the blood. Cases will be classified as: « Latent (early or late) spinal fluid negative » or « Latent (early or late) - spinal fluid not performed (diagnosis tentative) ». The date of the negative examination of the spinal fluid will be stated in all cases.

4. TERTIARY.

This classification is to be limited to cases that show active lesions of late syphilis. The lesion may be a gumma, or it may be a diffuse process and may involve any organ or tissue of the body. The majority of all patients with tertiary syphilis will fall within six categories:

a) *Mucocutaneous*. Late syphilitic gummatous lesions of skin or mucous membrane.

b) *Osseous*. Periostitis, osteomyelitis, arthritis, synovitis.

c) *Ocular*. Iritis, uveitis, keratoiritis, keratitis, chorioiditis, but not including optic atrophy.

d) *Visceral*. Hepatic, gastric, etc., but not including cardiovascular.

e) *Cardiovascular*. To include all lesions of the heart and great vessels; classify as follows:

(1) Aneurysm (saccular). Do not use for a fusiform dilation of the aorta. Specify artery involved.

(2) Aortic regurgitation (aortic insufficiency). Specify whether with or without cardiac decompensation.

(3) Aortitis, uncomplicated. To be used only for those patients with symptoms and physical or roentgen-ray signs of syphilitic aortic involvement in the absence of aneurysmal sacculation of aortic regurgitation.

f) *Neurosyphilis*. To include all cases with involvement of the central nervous system, classified as follows:

(1) Asymptomatic. To be used only for those patients with early or late syphilis who have no symptoms or detectable physical signs of central nervous system involvement, and in whom the diagnosis is based on the routine finding of abnormalities in the spinal fluid.

(2) Acute syphilitic meningitis. Usually occurs within the first two years of the disease, most commonly as a relapse phenomenon (neurorecurrence), manifested by the usual signs of low grade meningeal involvement, with or without cranial nerve palsies.

(3) Diffuse meningovascular. This is a catch-all classification to include all patients with neurosyphilis who do not fit into other diagnostic categories enumerated. Manifestations to be stated in each instance.

(4) Optic atrophy. Primary or secondary.

(5) Tabes dorsalis. Manifestations to be stated.

(6) Taboparesis. To be used only in patients with definite psychiatric signs of paresis complicated by definite clinically demonstrable evidence of damage to the posterior columns of the spinal cord.

(7) Psychosis with syphilitic meningo-encephalitis (general paresis). To be limited to cases which show psychic changes in addition to neurologic signs and the characteristic changes in the spinal fluid. Cases with parietic type spinal fluid but without psychic changes will be reported as : « Syphilis, diffuse meningovascular, manifested by..... ».

(8) Psychosis with neurosyphilis. To include neurosyphilis with psychosis other than cases of paresis and tabopareis.

g) If tertiary manifestations occur which do not fit into one of these categories, diagnose as:

« Syphilis, tertiary, otherwise unclassified » - Specify.

5. TYPE UNDETERMINED. To include cases in which accurate diagnosis has not been made. Every effort should be made to make a complete examination and proper diagnostic classification in all cases.

6. CONGENITAL. To be limited to cases that show

definite evidence of the existence or former existence of the characteristic changes of congenital syphilis, such as interstitial keratitis, Hutchinson's teeth, saber shins and other bone changes, saddle nose, eighth nerve deafness and so forth. The congenital origin of syphilis is not to be assumed merely because the time and the circumstances of the infection cannot be ascertained and there is no scar of a primary lesion.

7. The suggested terms for various drug poisonings are intelligible as they stand.

8. SPINAL PUNCTURE FOR DIAGNOSIS OR PROGRESS. This should be used in all cases (syphilitic or otherwise) routinely hospitalized for purpose of a spinal puncture.

For the SURGEON:

WILLIAM S. STONE
Colonel, M. C.,
Acting Deputy Surgeon.

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